PATHOBIOLOGY MICROBIOLOGY SUMMARY

SideKick

YOUR BEST FRIEND

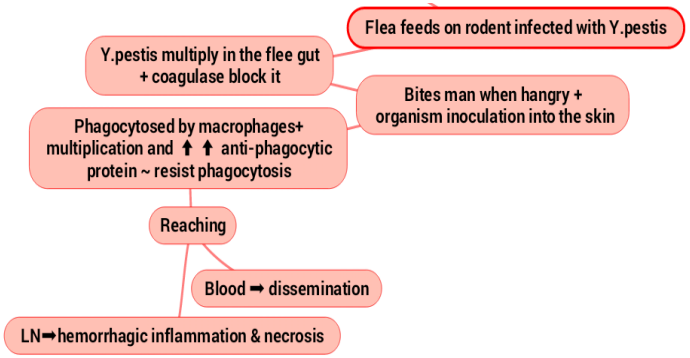
Bacteria

	Yersinia pestis {plague}	Yersinia enterocolitica {diarrhea}	Bacillus anthracis Anthrax	C. tetani	C.perfringens	Neisseria meningitidis
Morphology	✓ Gm-ve bacilli ✓ Capsulated at 37oC(at tissue) and non-capsulated at flea temperature ✓ Bipolar staining with Wayson stain pin like appearance ✓ **Non motile**, non-spore forming	✓ Gm-ve bacilli ✓ Non-spore forming bacilli ✓ **Motile** at 25 **and non-motile** at 37 degrees	- Gram+ve bacilli , Non-motile arranged in chains - Has polypeptide capsule Spores are oval and central in position	- Slender, **motile**, Gm+\ve rods - Spores placed at one end giving a **drumstick** appearance	- Large, Gm+ve bacilli **non motile**. - Spores are oval &The bacilli are often **capsulated in tissues**	- Gm-ve diplococcic - flattened & concave at sides "bean-shaped" - Intra PMNLs
Culture	- Facultative anaerobe - Grow better at 25 than 37 degrees - NLF on McCoy's agar - Definitive identification by immunoflurecent		- Aerobe and facultative anaerobe. - Grows on ordinary media at 37 °C. - On agar ➔ grayish, granular, circular discs resembling a hair lock (Medusa head appearance)	- Strict anaerobe - They grow on ordinary media & on blood agar swarming &haemolysis. - The organism grows readily on cooked meat broth	✓ Anaerobe & Grows best on CHO containing media. ✓ On horse blood agar, ➲ double zone of hemolysis; - a zone of complete hemolysis - a darker zone of incomplete hemolysis	- Anaerobe - Grow at 37º - needs (5-10%) CO2 - grows better on blood containing media - selective media ➔ Thayer-Martin
	**Grow rapidly on blood and fluid medium and slowly on solid medium =48 hrs.					

Biochemical tests	I CO U (- + - -)NLF ✓ Indole –ve ✓ Catalase +ve ✓ Oxidase –ve ✓ **Urease –ve** ✓ NLF on McCoy's agar	CO U (+ - +)NLF ✓ Catalase +ve ✓ Oxidase –ve ✓ **Urease +ve** ✓ NLF on McCoy's agar	1. Ferment sugar with the production of **acid only➔** saccharolytic 2. Catalase **+ve** **Liquefy gelatin** giving the "inverted fir-tree" appearance	❶ **asaccharolytic** ❷slowly **liquefy gelatin**	❶ (**Saccharolytic**). ❷ In **cooked meat broth**➲ medium is reddened with sour smell. ❸ Grows in **litmus milk medium** producing acid and gas **"stormy clot" reaction**. ❹ Grows on **egg-yolk medium** producing zones of opacity due to lecithinase activity ➔(**Nagler's reaction**)	✓ Oxidase +ve ✓ acid production from glucose & maltose
Virulence factors	PLC 1- **P**lasminogen-activating protease➔it is temp. dependent : **coagulase at: 20-28 D. flea temp.➲(Blocking) **fibrinolytic at: 35-37 D. Host temp. ➲(Dissemination) 2- **L**ipopolysaccharides ➔endotoxin 3- **C**apsule➔anti-phagocytic activity		1. **An extracellular toxin** {protective antigen, lethal factor, and edema factor}➔**cytolytic to** macrophages➔ causing edema and shock ➔biologic warfare. 2. **Capsular polypeptide➔inhibits opsonization** and **phagocytosis**	** Toxins produced by C. tetani: ❶**Tetanospasmin**: is a very potent toxin, extremely small amounts ➲ lethal for humans. ❷ **Tetanolysin**: is an oxygen-labile hemolysin.	**There are 5 types of C. perfringens (A-E) ❶ **Alphatoxin (lecithinase)➔destroy cell membranes**. ❷**Hyaluronidase, collagenase➔ spread of infection**. ❸ **Enterotoxin➔** by C.perfringens which cause food poisoning (type A➔**alters the permeability of the enterocyte**	1- pilli → adherence 2- polysaccharide capsule → anti-phagocytic 3- outer membrane protein → adhesion 4- lipo-polysaccharide → antitoxin 5- IgA protease

Pathogenesis

Yersinia pestis {plague}:



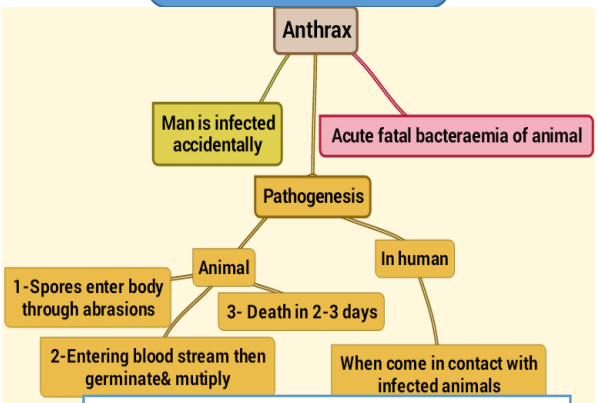
Yersinia enterocolitica {diarrhea}

- Ingestion of contaminated food and drinks with y. enterocolitica which is present in the intestine of animals: cattle, sheep's…↓
- Man become infected↓
- Suffer from **acute enterocolitis**

Neisseria Meningitidis

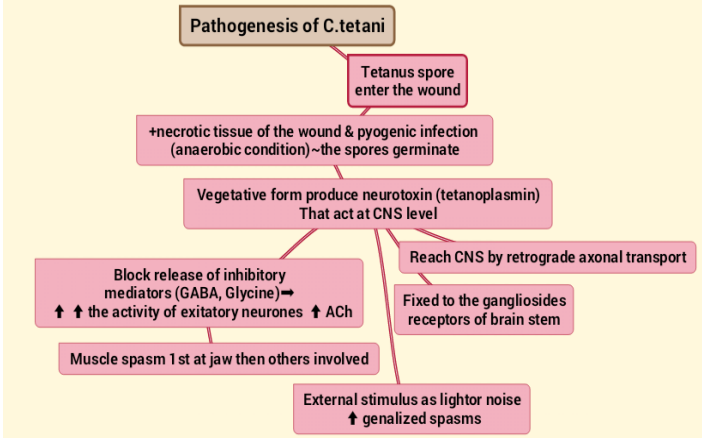
- Droplet from patient / carrier …↓
- Man become infected↓
- the organism attaches itself to cells of nasopharynx
- It may enter blood stream

Bacillus anthracis "Anthrax"



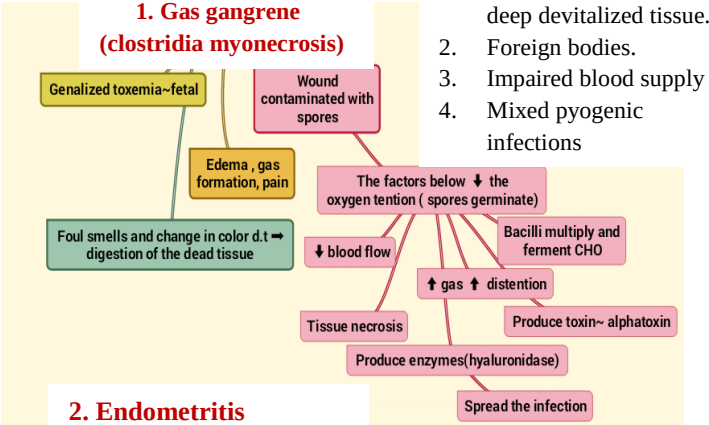
*Plague is an infection of rodent transmitted between them and to man by fleas' bites
Cause millions fatalities ➔ **Black Death**
*Death usually results from interference with the mechanics of respiration.

C. tetani



C. tetani is **non invasive

C.perfringens



Infection of a post-partum uterus ➲necrosis of uterine tissue➲ intravascular hemolysis ➲ septicemia

***Factors which help spore germination are**:

1. Traumatic wounds with deep devitalized tissue.
2. Foreign bodies.
3. Impaired blood supply
4. Mixed pyogenic infections

Clinical Picture

Yersinia pestis			Yersinia enterocolitica	Bacillus anthracis		C. tetani	C.perfringens	Neisseria meningitidis
Bubonic plague	**Pneumonic plague**	**Septicemic plague**	**Acute enterocolitis	Cutaneous anthrax (malignant pustule)	Inhalation anthrax *(Woolsorters' disease):* Haemorrhagic pneumonia Gastrointestinal anthrax Injection anthrax	1. Muscular spasms at site of infection 2. jaw lock 3. interference with mechanisms of respiration	Gas gangrene Endometritis food poisoning	1. Bacteremia: Occurs in small percentage of patients 2. Meningitis: Organisms reach through blood → meninges ➔ multiply ➔ acute inf. response (↑↑ PMNLs) ➔ purulent meningitis 3. Joint symptoms & petechial rash ***"PATHOGNOMONIC OF MENINGOCOCCAL MENINGITIS"*** • Headache – vomiting – fever – stiff neck - coma
- lymphatic gland of groin swell, V.painfull - mortality rate 50-70%	Primary (direct inhalation) , severe respiratory distress& mortality rate 100% - Secondary (metastatic from bubonic)	- High level of bacteremia before buboes - Symptoms very sever& poor prognosis - Mortality rates 100%	1. Fever 2. Abdominal pain ➲ at right lower quadrant as appendicitis 3. Diarrhea(watery) 4. Heat stable enterotoxin invade blood& LN	Spores enters through abrasions in the skin ↓ The spores germinate multiply ↓ ➔At the site of entry a papule ➔vesicle➔ pustule ➔necrotic black crusty ulcer **characteristic central black eschar ➔ Death				

Lab diagnosis

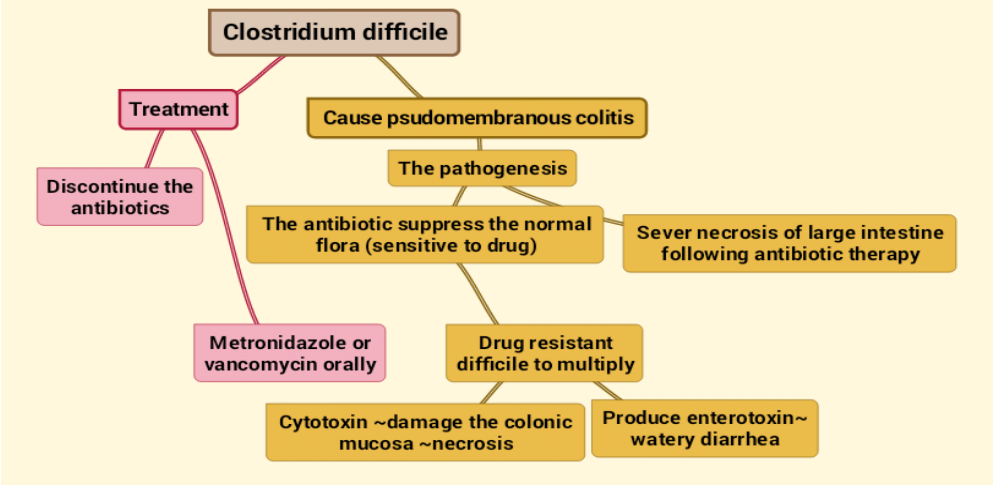
1) Specimen ➔aspiration from the enlarged LN. 2) EM ➔film shows short Gm-ve bacilli	1) Specimen: patients sputum **2, 3,4 as the ➲ Bubonic plague	1) Specimen Blood **2, 3,4 as the ➲ Bubonic plague	1. Specimen ➔aspiration from the enlarged LN. 2. Cold enrichment ➔film	✪ Specimen ➔fluid from vesicle. ✪ Smear ➔ large gm+ve bacilli spores are not present	Specimen➔ Sputum or pleural fluid are obtained 2, 3,4 as the ➲ malignant pustule	A. **Clinical** (Mainly) ➲once as tetanus, treatment with antitoxin should start at once	**Clinical (mainly) Laboratory**: Specimen: wound exudates particularly from the deeper parts where the infection seems to	Specimen➔ CSF, blood, aspirate from nasopharyngeal swab Smear ➔ neisseria inside PMNLs

3) Culture ➔ blood agar, maCconky's then biochemical& immunoflurecent. 4) Serology In un-vacinated patient titre 16 suggestive& Rising titre diagnostic			shows short Gm-ve bacilli 3. Culture ➔ **maCconky's➲NLF** 4. Biochemical tests: CO U (+ -+)NLF	✪ Culture ➔*Colonies ➲medusa head {Nutrient agar}. *Colonies ➲ non-hemolytic on{blood agar}. ✪ Definitive identifi-cation *Detection ➲capsule by fluorescent antibody *Identification of toxin genes by (PCR)		**B. Lab Diagnosis** -Specimen: wound exudates Gram-stained smear: drum stick appearance. -Culture **Into cooked meat**: growth leads to **blackening** of the medium. **Onto blood agar**, incubated anaerobically, it shows a **swarming** growth and **haemolysis** (due to tetanolysin). Identification A) Biochemical tests b)Animal pathogenicity test: ➲➲**The unprotected animal dies of tetanus while the protected control remains alive**	be most pronounced. Direct Gram-stained smear: The presence of large Gram positive rods is suggestive Culture : On blood agar incubated anaerobically. Identification: BY *Morphology *Biochemical tests as mentioned before. *MALDI-TOF MS: is a rapid and sensitive method for identification of invasive Clostridium species recovered in culture	Culture ➔ Oxidase +ve Gm film Acid production Serotyping ➔ agglutination Non - Culture ➔ PCR Latex agglutination

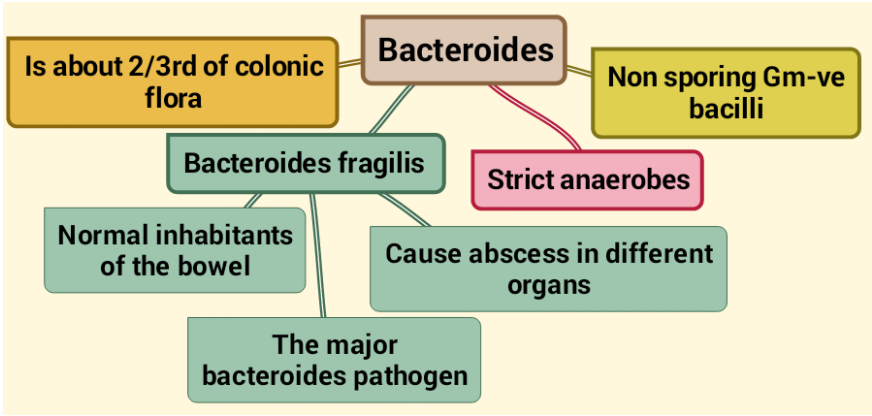
Prevention				
Yersinia pestis	**Bacillus anthracis**	**C. tetani**	**C.perfringens**	**Neisseria meningitidis**
1. Vaccination : killed whole-cell vaccine was used, others are under development **Chemoprophylaxis: Doxycycline**	1. Disposal of animal bodies 2. Decontamination 3. The use of gloves when handling infected material. 4. Immunization of domestic animals. 5. Vaccination of people working with animals with toxoid	**(1) active immunization with toxoids**; - "DPT"{ tetanus toxoid, pertussis vaccine & diphtheria toxoid}➔3 **IM** injections at 2,4 and 6 months with a booster dose is given a year later and another upon entry into school. - A booster dose of (TD) is recommended every 10 years - Booster doses are given to military personnel & for pregnant women. **(2) prophylactic use of antitoxin IV**; ❶ antitetanic serum **(ATS)** after skin test, obtained by immunizing horses with toxoid ❷Human tetanus immunoglobulin **(HTIG** (3) Proper **care of wounds** contaminated with soil. (4) Administration of **penicillin**.	1. Administration of **antibiotics** early 2. **cleaning** of wounds 3. **Removal of foreign** bodies 4. **Surgical** debridement 5. **Antitoxin** for prophylaxis is **unreliable**. **X** 6. **Toxoids are not available** for active immunization. **X**	1. Detection of carriers: nasopharyngeal swab → culture on Thayer-Martin medium ➔ if +ve → Rifampin ➔ Ciprofloxacin → adults ➔ Ceftriaxone → children 2. Avoid overcrowded areas 3. Vaccines: • Trivalent polysaccharide vaccine • Trivalent conjugate vaccine • 2 new serogroup B vaccines

Treatment					
Yersinia pestis	**Yersinia enterocolitica**	**Bacillus anthracis**	**C. tetani**	**C.perfringens**	**Neisseria meningitidis**
** combination streptomycin+ doxycycline for 10 days *Ciprofloxacin may be used	- 3rd generation cephalosporin in severe cases+ aminoglycosides	- Penicillin G (early) - Ciprofloxacin - Recombinant human monoclonal antibody➲ Inhalational anthrax	- Patients with symptoms of tetanus ➲ nonspecific supportive measures {dark environment, muscle relaxants}. - A very large doses of antitoxin (HTIG IV if not available, AST is given in bigger doses ½ IV and ½ IM}	- Surgical debridement, Amputation may be needed. - Penicillin in large doses. - Hyperbaric oxygen therapy ➲ oxygenates tissues which are hypoxic. - Antitoxic sera +/-	• Penicillin G • Chloramphenicol • 3rd generation cephalosporin

Clostridium difficile



Bacteroides



Superficial & Opportunistic Mycosis

1) Dermatophytes

1. **Geophilic dermatophytes:** contact with soil.
2. **Zoophilic dermatophytes:** contact with infected animals.
3. **Anthropophilic dermatophytes:** contact with infected humans.

	Microsporum	**Trichophyton**	**Epidermophyton**
Species	14	20	1
Macro-candida	Multiseptate, variable in forms, big sized, thick wall & irregular surface	Thick wall, clavate to fusiform in shape	Thick wall, smooth surface, clavate, oval or pyriform in shape
Micro-candida	Present	Spherical, pyriform, irregular in shape & size	Absent
Affected organs	Skin – hair	Skin – nail – hair	Skin – nail
Examples	M. Canis M. Audouinii M. Gypseum	T. Rubrum T. Violaceum T. Mentagrophytes	E. Floccosum

Dermatophytid: formation of sterile itching lesions on body sites distant from point of infection.

2) Pityriasis Versicolor (Tinea Versicolor)

- lesions in epidermis which are non-contagious, non-inflammatory with branny scales.
- causative fungus: pityrosporum orbiculare = malassezia furfur
- It's a lipophilic fungus

* Difference between onychomycosis & Tinea unguinum:

Onychomycosis:	**Tinea unguinum:**
Infection of nail – nail beds Mostly caused by dermatophytes, but can be also caused by other fungi.	Caused exclusively by dermatophytes

Opportunistic fungal infections

1) Aspergillosis

- Fungal infection caused mainly by genus aspergillus.
- The clinical picture is dominated mainly by respiratory manifestations

Causative agents: FnFn

- A. Fumigatus → 90%
- A. nigra → 5%
- A. Flavis → 4%
- A. nidulans → 1%

2) Candidiasis

* It results in superficial and disseminated mycosis
* Candida albicans is the most common frequent etiologic agent
* It is common in micro flora of the atmosphere – saprophyte in the alimentary tract and vagina of 10-50% of healthy people.

Predisposing factors to candidiasis:

A- Internal factors:

I- Physiological:
- Pregnancy
- Infancy & old age
- Obesity

II- Pathological:
- Debilitation
- Neoplasms (especially lymphoid ones)
- Endocrinopathy (DM)
- Autoimmune disease
  "chronic mucocutaneous candidiasis"

B- External factors:
- radiotherapy
- drugs: antibiotics & cytotoxic drugs
- surgery
- peritoneal dialysis
- drug addiction (IV ingection)

3) Cryptococcosis "Cryptococcus neoformans"

* It causes pulmonary and meningeal infections, it's present mainly in pigeon excreta.

Morphology:

Spherical yeast, reproducing by budding, surrounded by large mucoid polysaccharide capsule.

Epidemiology:

Occurs frequently in males,

Exposure to pigeon excreta is the most common cause.

Immunity:

- Capsule is a very important virulence factor, "inhibits phagocytosis"
- Cell-mediated immunity is important to resist infection

Humoral immunity has no role against the infection

4) Zygomycosis "Zygomycetes"

* They are primitive, fast growing saprophytic fungi.

They include 2 genera:

a- Mucor

b- Rhizopus

	Dermatophytosis	Pityriasis Versicolor	Aspergillosis	Candidiasis	Cryptococcosis	zygomycosis
Clinical Presentation	Infections of Hair and Hair Follicles: 1-Tinea Favosa:- Caused by T.Shoenleinii ❖ Infection of Hair Follicles ❖ Crusty lesion made of dead epithelial cells and Fungal mycelia "Scutula" ❖ Permanent hair loss and scar tissue formation. 2-Gray patch ring worm caused by M.audouinii and M. canis ❖ Infection of Hair Follicles then Shafts from inside " Ectothrix" ❖ Mainly in Childhood 3-Black dot ring worm caused by T.Tansurans T. Violecia ❖ Infection of Hair Follicles then Shafts from inside " Ectothrix"	❖ Interference with the normal pigmentation of the skin ❖ Ocular May be -primary as cerebral aspergillosis. -Secondary due to abuse of antibiotics. →Corneal ulcer ❖ Onychomycosis Very common disease	A- Pulmonary aspergillosis B- Disseminated aspergillosis: Spread : by blood Diagnosis : 1-serological tests 2-Histo-pathological examination C- localized aspergillosis: 1-Endocarditis -after open heart surgery . -diagnosed by :- Electro-cardiography Serological tests. 2-cerebral abscess:' -Metastasis by blood -surgical operation -direct infection From nasal sinus	GIT Candidiasis:- -oral -Esophageal -Enteric (less commonly diagnosed ante-mortem) 2-Bronchial Pulmonary 3-Candida endocarditis very common 4-Renal candidiasis -candiuria benign colonization. -True infection Can lead to pyelonephritis and cortical renal infection. 5-Vaginal and vulvo vaginal candidiasis During pregnancy in diabetic patients.	❖ Involvement of CNS is more frequent than lung involvement. ❖ After pulmonary affection ,hematogenous spread occurs to various organs Predisposing factors -AIDS - Reticulo-endothelial malignancy	❖ The most acute fulminant fungal infection known . ❖ Rhino-facial-cranial area is affected **It has many predisposing factors** -Diabetes -Starvation -severe burns -IV addiction -Leukemia -Lymphoma

	❖ Breaking of hair shafts beneath the scalp Infection of Nail-Nail bed: Caused by T.Tansurans T.rubrum T.mentagrophytes Athlete's Foot T.rubrum T.interdigitale		3- Bone abscess: Direct extension from maxillary sinus -invasion by blood - infiltration by corticosteroids 4-Cutaneous infections AIDS patients Invasion by blood stream 5-Sinusitis Very common in Sudan A.Flavus Mainly affect maxillary sinus may lead to proptosis. 6-otomycosis A.Niger Very common in Egypt	6-Candida septicemia. 7-Candida meningitis (Newborn infants) 8-Candida intertrigo:- Due to exposure to heat and humidity and to tropical moisture. 9-Onychia-Paronychia: Chronic infection due to immersion of hands in water. 10-chronic mucocutaneous candidiasis Children under 6 ys due to congenital cellular immunodeficiency.		

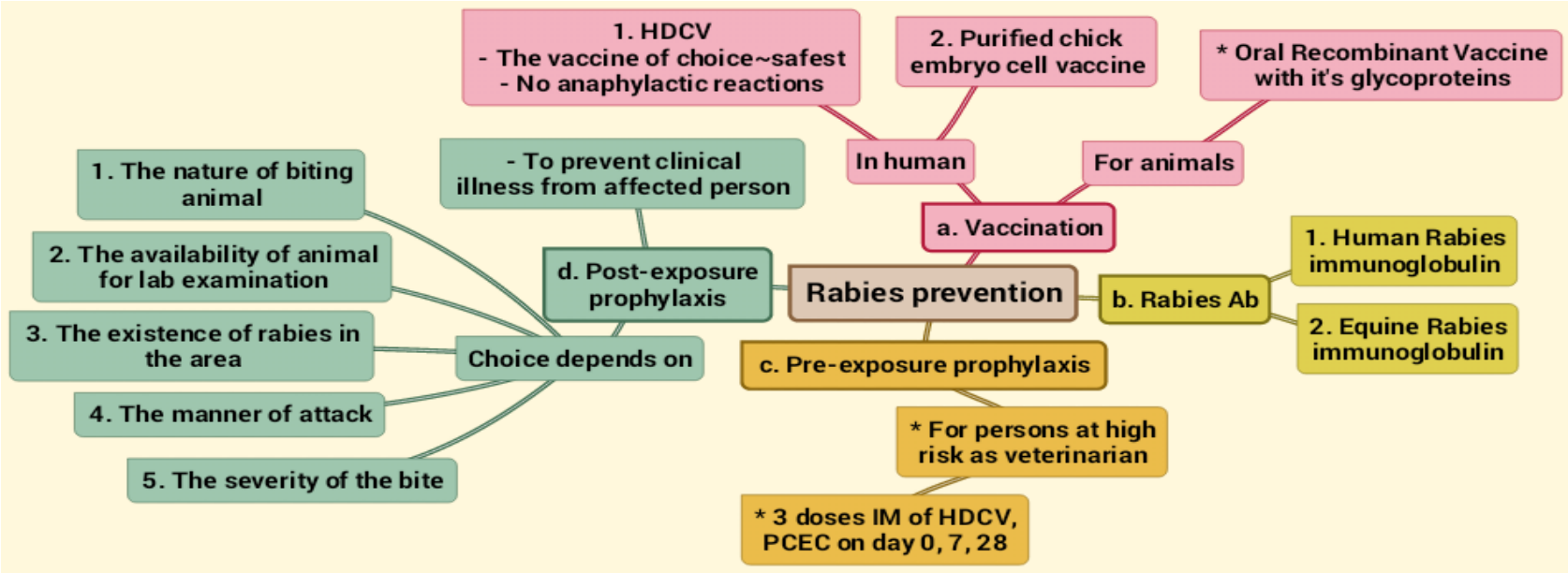
Lab Diagnosis	Specimen Skin Scales-Hairs-Pieces of nail. Direct Microscopy -Add KOH(10-30%)to soften and clear the specimen. -Branching hyphae and chains of arthrospores are seen . -In case of hair you have to see if it is outside the hair shaft or inside. Culture On SDA with chloroamphenicol +Actidione to kill saprophytes. Grow at room temp.for 3 weeks	Specimen Adhesive tape is applied on the infected skin then to the slide or collect scales with blunt scalpel. Direct Microscopy Hyphae are short ,curved are rarely branching with spherical cells. Culture Budding yeast like cells	Specimen According to the lesions examined. Direct Microscopy Appear as septate hyphae with angular dichotomous branching. Culture Conidial morphology and color on SDA Serology Ag detection Ab detection Molecular Technique PCR	Specimen According to the lesions examined. Direct Microscopy Budding yeasts and pseudomyceluim Culture Yeast like colonies Antigen assays Identification of C albicans -Germ Test tube -Rice agar tween test -Fermentation and assimilation test Histopathological examination Blastospores and pseudohyphae can be demonstrated Serology Detection of antibodies Molecular Technique PCR and probes	Specimen CSF-sputum-serum-urine. Direct Microscopy -Round or oval organisms budding. -India ink will reveal the capsule. Culture On SDA Shiny mucoid colonies. Under microscopy Appear as spherical yeasts with buds -can assimilates glucose, maltose, sucrose but not lactose -Urease + Serology Detection of antigen Histo-pathological examination Appear as pale blue often thin walled spherical or oval bodies with a clear halo around.	**Specimen** Sputum-nasal dicharges-scrapings. **Direct Microscopy** Broad non septate thin walled hyphae with focal bulbous dilations And irregular branching. **Culture** On SDA (white to grey cottony colonies **serology**
Treatment	1-Keratinolytic agents 2-Local Ontiments: Clotrimazole,Miconazole 3-Oral drugs: -Griseofulvin - fluconazole -Itraconazole -terbinafine	1-Keratinolytic agents 2-Loca:l Clotrimazole, Econazole 3-Oral drugs: fluconazole	1-Itraconazole 2-voriconazole 3- AmphotericinB (nephrotoxic)	Polyene group Imidazole derivatives	Combined drug therapy 1-Flucytosine +amphotericin B 2-Fluconazole +amphotericin B	AmphotericinB Newer drugs Posaconazole

Rabies, Parvovireses, Arbo & Robo viruses

	Rabies virus	Parvoviruses	JC virus & BK virus
Family	**Rhabdoviridae**	**Parvoviridae**	**Polymavirus family**
Properties	- Bullet shape, SS RNA virus - Enveloped with glycoprotein spikes - Has ribonucleocapsid	- They are the **smallest** DNA animal viruses - Icosahedral, non-enveloped particles, SS RNA virus. - Viral replication is dependent by coinfecting helper virus.	- Small non enveloped viruses - Cubic symmetry. - The genome is circular, DS DNA
Pathology &mode of infection	❶ it multiplies in muscle ➲ peripheral nerves➲ multiply CNS {Encephalitis} ❷Spread to the salivary gland and other tissues (cornea, kidney… ☆ highest titre ➲submaxillary salivary gland ☆cannot be isolated from blood of the infected person ◆◆ incubation period depends on: - Virus conc. & severity of wound - Distance from entry to CNS - Host age and immune system	✓ The only recognized human pathogen in this group of viruses is the Parvovirus B19 ✓ Infection is common in childhood ⊙ ***Mode of infection:*** 1) **Respiratory** route. 2) The virus can be transmitted **parentally** by blood transfusions➲ the principal target for B19 3) **vertically** from mother to fetus	1) BK and JC viruses' infection usually occurs early childhood. 2) Both viruses may persist in the kidneys & lymphoid tissues of healthy individuals after primary infection 3) may reactivate when the host′s immune response is impaired
Clinical picture	❶ **In human**(incubation period 1-3 months) 3 phases : ⊙ short incubation phase: - Lasts 2-10 days with no specific symptoms: (headache, anorexia, N, V, **photophobia** &abnormal sensation at the site of the bite) ⊙acute neurologic phase: - Lasts 2-7 days with neurological dysfunction (hallucination, over-activity, papillary	❶ ***Erythema infectiosum (fifth disease)***: **children** - The most common of B19 & associated with a faint rash➲ the face has a "**slapped cheek"** appearance. - Joint involvement is a prominent feature in adult cases. ❷ ***Transient aplastic crisis***: - may complicate chronic haemolytic anaemias e.g. sickle cell anemia,	❶ ***(BK)*** 1) ***Nephropathy*** usually happens in 5% of kidney recipients 2) BK ***hemorrhagic cystitis*** in patients with bone morrow transplantation. ❷ ***JC virus*** 1) ***(PML)*** occurs in some immunocompromised patients 2) JC virus has been recently associated with human ***brain tumors***

<table>
<tr>
<td></td>
<td>dilatation, increased salivation, hydrophobia & painful spasm of throat muscle
⊙ <u>coma phase</u>:
Convulsion , coma, death D.t cardiorespiratory arrest
❷ in dogs(incubation period 3-8 Weeks)
Divided into 3 phases as in man</td>
<td>thalassemia decrease red cell synthesis in the bone marrow
❸ chronic suppression of the bone marrow
Called pure cell aplasia ➲ in immunodeficient host
❹ during pregnancy may result in hydrops fetalis and fetal death in due to severe fetal anemia ➲abortion occur</td>
<td></td>
</tr>
<tr>
<td>Lab diagnosis</td>
<td>❶ In human:
⊙ <u>cytopathology</u>:
- The presence of Negri bodies➲ specific eosinophilic intracytoplasmic inclusions with viral nucleocapsid
⊙ <u>detection of rabies Ag or NA</u>:
- Using immunofluorescence by monoclonal Ab
- RT-PCR: amplify part of the genome
⊙ <u>viral isolation</u>:
- Brain examination after encephalitis death of mice for rabies ag and Negri bodies
- Mouse culture cell line with rapid growth of rabies virus which is identified by fluorescent antibodies
⊙<u>serology</u>:
<table>
<tr><th>Serum ab (immuno-fluorescence)</th><th>CSF ab</th></tr>
<tr><td>- Slowly developed in infected person
- Quickly detected in vaccinated person</td><td>- Detected in rabies infected person
- Not detected in vaccinated person</td></tr>
</table>
❷ in dogs:
- Should be sacrificed for lab examination
- Others are hold for 10 days if encephalitis occur they should be killed for examination</td>
<td>- Virus is difficult to glow = <u>cannot be isolated</u>
- The most sensitive tests are DNA detection by <u>PCR</u>, NA probes
- <u>Serology</u> to measure ab:
*B19 IgM➲ recent infection✧ persist for 2-3 months
*B19 IgG➲ recovery ✧ persist for years
*** not detectable in immunocompromised person
- Ag detection assay
- In fetal infection ➲ PCR analysis of amniotic fluid</td>
<td>1) <u>Cytopathology</u>
Urine samples can reveal the presence of JC & BK viruses ➲ showing enlarged cells with intra-nuclear inclusions.
2) <u>Polyoma antigens</u> may be demonstrated in infected cells by IF.
3) <u>PCR& N.A. probes</u> can detect viral N.A.
4) <u>E.M.</u> can be used to visualize VIRUSES particles in brain tissue in case of PML</td>
</tr>
</table>

Prevention	***⊙⊙ SEE THE DIAGRAM BELOW ↓↓*** ** This depends on decrease the chance for viral replication and CNS invasion. • **Frist Protective measure:** - Wound cleaning with soap and water - Stitching should be avoided - Instillation of Rabies immunoglobulin the wound (HRGH passively till respond to HDCD, PCEC actively to produce ab). • **vaccination and doses:** ❶ immunocompetant: 4 doses at day 0,3, 7, 14 ❷immunocompromised: 5 doses at day 0,3, 7, 14, 28	1) Immunoglobulin for immunocompromised patient with chronic B19 infection 2) There is no vaccine. 3) Good hygiene as hand washing can prevent B19 spread through respiratory secretions	……
Treatment	✓ No specific treatment only symptomatic ✓ Interferon, ribavirin has no beneficial effects	✓ Fifth disease➲ treated symptomatically ✓ Severe anemia ➲ transfusion therapy	……..



Slow virus infection & prion disease (transmissible spongiform encephalitis)

Definition & pathogenesis

- ✓ Chronic degenerative disease caused by slow, chronic persistent infection by classic viruses
- ✓ "slow" is the rate of progression and not the rate of replication
- ✓ Characterized by: "long" incubation period, "gradual" onset& "fetal" progress

- ✧ Degenerative CNS diseases
- ✧ The causative agent is not a conventional virus but proteinaceous material with no DNA or RNA➲**Prion** which is only composed by single glycoprotein that encoded by the host cell
- ✧ Conformational change to the disease form (**PrPSc**) ➲ causing neural cell death
- ✧ PrPSc has the ability to interact with **PrPC** converting it to the disease form (**PrPSc**)

Features:
- Neural degeneration and vacuolation
- Amyloid accumulation

Characteristics : **4 NO**
- ✓ "long" incubation period followed by➔ **no** remission& **no** recovery
- ✓ **No** inflammatory response & **no** immune response

Clinical picture

In animal

✪***Visna :***
- Chronic progressive neurological disease of sheep
- Caused by: retrovirus
- **Characterized by**: All organ are affected specially : brain, lungs& RES

"long" incubation period, "SLOW OR RAPID" progression

✪**Scrapie:**
- ✓ Disease of sheep
- ✓ **Characterized by**: tremors , ataxia &itching ➲ the sheep scrape off their wool against wall

✪**Bovine spongiform encephalopathy(BSE): (mad cow disease)**
- **Acquired by**: eating cattle feed supplemented with organs as brain obtained from sheep infected with Scrapie prions

In human

✪***Subacute sclerosing panencephalitis (SSPE):***
- Slow progressive CNS demyelination in patient early infected by measles
- **Characterized by**: Progressive mental depression , involuntary movement, muscle rigidity

❍ **measles ab** in CSF, SERUM & **measles particles** in brain tissue

✪**Kuru:**
- Fetal disease with progressive tremors and ataxia
- Spread by cannibalism of dead relative and has disappeared

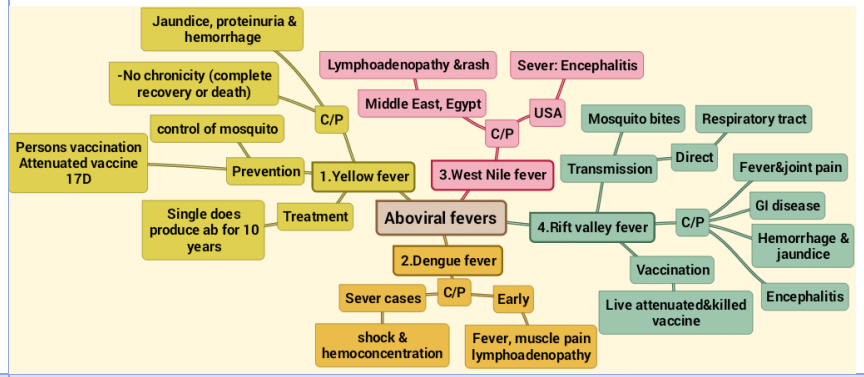
✪**Creutzfeldt-jakob disease:**
- ✓ Associated with: dementia &myogenic jerking and progress into death
- ✓ Sporadic mainly with 15% hereditary

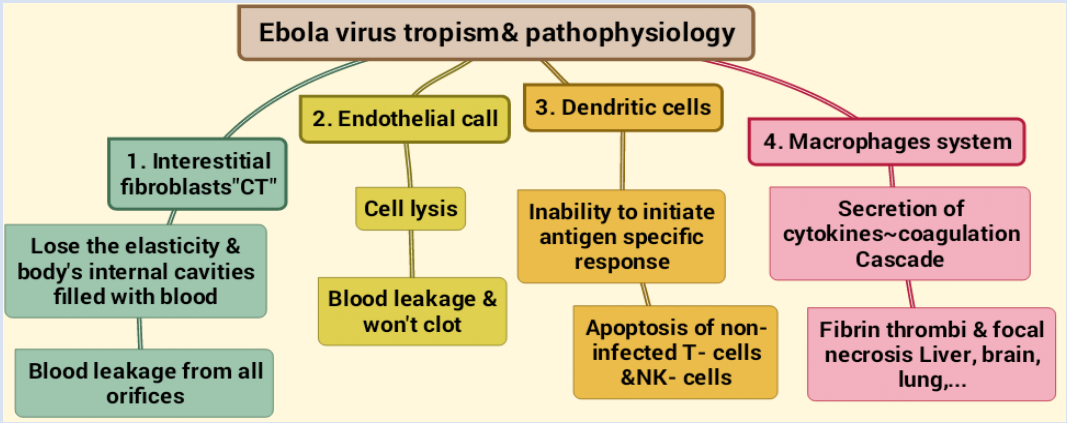
❍**Transmission by:**
- GH from cadaver pituitary
- Corneal transplantation & dura matter graft
- Contaminated Surgical instruments & ECG electrodes

✪ ***Progressive multifocal leukoencephalopathy (PML):***

Fetal demyelination of white matter of the brain in multiple sites
Occurs mainly in immunocompromised patients ➲AIDS
Caused by: **JC virus** & **BK virus**
Characterized by: visual defect, mental change, blindness coma

✪**Variant Creutzfeldt-jakob disease**: occur in younger people
- ✓ It is a new variant of CJD & BSE caused by a common agent
- ✓ The pathological characteristic similar to BSE
- ✓ human infected through consumption of BSE contaminated beef

	Arboviruses	Arboviruses
Definition	Arthropods born viruses they are transmitted by blood **sucking arthropods** with lifelong infection with no damage to themselves	Persistent infection in rodent transmitted between rodents **without** arthropod vector
Cycle and biological transmission& Pathogenesis	Triad : vector, vertebrate host & viruses ** when female mosquito feeds on blood ➲ mid gut ➲ multiply **{1ry viremia}** ** tissue invasion (salivary gland)➲ multiply ➲**2ndry viremia** Most ➔ subclinical • Rash, pharyngitis or encephalitis & hemorrhagic fever With ***biphasic course*** - Primary viremia followed by remission - Recrudescence of pyrexia ➲ 2ndry viremia + encephalitis Fever + haemorrhage =haemorrhagic fever	Transmission by - Direct contact with body fluid or rodent excreta - Inhalation of dust containing rodent excreta
General characters	- have biological method for transmission - RNA viruses - Ether sensitive	…….
Examples of infection	1- Encephalitis 2- Specific fevers: 	- Most of them produce haemorrhagic fever: ❶ Hantavirus : - * haemorrhagic fever& renal syndrome (renal failure) in Korea *pulmonary syndrome in USA ❷ Lassa fever virus ❸South America haemorrhagic fever ❹Ebola virus ➲Africa haemorrhagic fever ❺lymphocytic choriomeningitis virus: Roboviral infection **not cause** haemorrhagic fever
Treatment	……	Supportive with IV ribavirin

Characters	Zika virus Arboviruses & Highly aggressive spread	Ebola virus Arboviruses
Reservoir	…..	Rodents & fruit bats
Virulence factors	……	1- Secretory glycoprotein➔ bind with neutrophils and inhibit their activation and so rapid dissemination of the virus 2- Two other proteins➔ suppress the interferon response
Incubation period	3-12 days	2-21 days
Pathogenesis	……	
C/P	✓ Most cases with no symptoms ✓ Mild resemble dengue fever ✓ Symptoms: Fever, rash, conjunctivitis…	✓ Early: fever , headache ✓ Followed by: abdominal pain V, D and bleeding {internal& external} ✓ Late: shock& death *** No specific treatment only supportive
Transmission	- Mosquito bites - From pregnant women to fetus: ** congenital abnormalities, microcephaly, trigger Guillain-Barre syndrome - Sexual contact - Blood transfusion	1. Person to person 2. Nosocomial 3. Laboratory infection

HIV

Morphology:

- Enveloped single stranded RNA virus

- The nucleocapsid is formed of :-
  a- 2 identical strands of RNA cerry genes
  -Gag gene
  -Pol gene
  -pro gene
  -Env gene
  b- Enzymes (RT-P-I)
  c- Structural protein : p24

- On the envelop , these are gp 120-40 (gp120) surface .. (40)transmembrane

Look at the book

Pathogenesis:

1- Virus affects CD4+ve cells
(t4 lymphocytes – macrophages – monocytes)
and also some CD4-ve cells
(renal –GI epithelial cells – brain –astrocytes)
2- Macrophages → qualitatively affected
t4 lymphocytes → qualitatively – quantital affected

Clinical picture:

1- Primary infection (acute retroviral infection)
- ↑viremia
- The patient is highly infections
- Virus is widely disseminated acute mononucleosis like syndrome .

2- Asymptomatic chronic infections (clinical latency) :
- Patient is asymptomatic

virus is replicating – infecting other cells

Transmission:

1- Horizontal transmission :
   A. sexual transmission
      "especially if there is genital lesion ,ulcesrs "
   B. blood and blood products
2- vertical transmission :
   A. congenital →transplacental
   B. intranatal → during passage along the birth canal
   C. breast feeding

Diagnosis:

1- immunologic features :
   great reduction in number of CD4 lymphocytes , low ratio of t-helper
   → it drops (50-100 cells/mm3)
   → ›500 (clinical year latency)
   →200-500 (first degree of immunodeficiency)
   → ‹ 200 (frank AIDs)
2- viral antigen of N.A :
   -ELISA
   -PCR→most sensitive especially in newborn .
3- viral isolation :
   only in research centres .
4- Antibody essay :
   - EILISA is used in routine screening → if+ve test is repeated
   - To conferm →western blot technique (WB)

Immunoflourescent assay

Treatment:

1- Reverse transcriptase inhibitors :
   - Nucleoside RTI (NRTI)
   - Nucleotide RTI (NtRTI)
     ozidothymidine –tenofovir
   - NONnucleoside RTI :
     nevirapine (NNRTI)
2- Protease inhibitor (PI) :
   - Saquinavir – ritonavir
3- Integrase inhibitor :
   - Elvitegrevir (INSTI)
4- Receptor CCR5 antagonist :
   - Maravoric
5- Fusion inhibitor
   - Fuzeon

HAART

Highly active antiretroviral rheraby
- Compination theraby
  2 drug of NRTIs

1 drug of NNRTIs , PIs, INSTIS .

Herpes Viruses

	Varicella zoster	EBV
Important properties	☆ **DS DNA, icosahedral** ☆ **Enveloped,** ☆ **Single serotype**	
Transmission & epidemiology	✓ Direct contact with lesion ✓ Respiratory droplets	✓ **Saliva**
Pathology & immunity	1. Infect mucosa of the upper respiratory tract 2. Initial replication in the regional LN then spread via blood to the skin 3. Swelling, ballooning and degeneration of epithelial cells of the skin and accumulation of tissue fluid vesicles formation 4. During immunosuppression periods replication in the ganglia occurs, virus travel down to the nerve to the skin & induce vesicles formation	**1. Infect oropharynx** **2. Infect B cells and spread the infection through the body** **3. T-cell react against infected B-cell and for atypical lymphocytes** **4. Heterophile antibodies also appear which can agglutinate sheep and hours RBCs**
Clinical finding	1. Varicella: - Symptoms of fever, malaise& Papular rash **In immunocompromised children: - Encephalitis & pneumonia 2. Zoster: - Rash limited to the area innervated by that single nerve - Sever pain	**1. In children:** - **Usually silent and asymptomatic** **2. In adolescent:** - **Fever, sore throat** - **Lymphadenopathy, splenomegaly & hepatitis** **3. Reactivation is usually silent**

Diagnosis	- Cytopathology - Viral immunology - DNA detection	- **Blood smears➔ atypical lymphocytes** - **Serology➔specific EBV antibodies** - **DNA detection**
Treatment & prophylaxis	✓ No treatment ✓ LAV for varicella ✓ Herpes zoster vaccine: frequency& severity	✓ **No treatment** ✓ **No vaccines**